

REMARKS/ARGUMENTS

Provisional Election and Partial Traverse

Applicants provisionally elect to prosecute the invention of Group LXXI (claims 74-90) and traverse the requirement for restriction insofar as it applies to claims of Groups LXXI, LVII and LVIII, which include claims 74-90, 91-92, and 93-94, respectively.

Applicants also traverse the requirement for restriction insofar as it applies to the above Groups and Group LXX (claim 108).

For clarity, claims 74-94 have been replaced by new claims 113-133 by this amendment. The new claims define the compounds much the same as those replaced. However, claim 113 (which replaced claim 74) no longer includes compounds in which Q^3 is a moiety containing the group "E". In addition, to show that they belong to the same group, the compounds formerly included in claims 91-94 are now claimed via dependent claims from claim 113.

Claims 91-94 are deemed to define a common invention with claims 74-90. Claims 91-94 define the same types of compounds as claims 74-90, except that when R^C of claim 74 is a carboxyl, the compounds contain a carboxyl protecting group [Pg^C of claims 91 and 93]. The specification, p. 10 lines 9-11, in defining R^C , states that it is a carboxy terminal group that may contain a protecting group Pg^C . Accordingly, Applicants submit that these compounds are part of the same invention. To emphasize that, new claims 124-133 are dependent on new main claim 113 and define R^C as being Pg^C .

Claim 108 defines a library of peptide mimetics containing at least one mimetic according to new claim 113. Its coverage of compounds is thus contiguous in definition with claim 113, the search will be the same as for claim 113, and its inclusion in the elected invention is seen as proper.

Applicants thus request withdrawal of the requirement for restriction among Groups LXX, LXXI, LVII and LVIII.

Provisional Election

In response to the requirement for election on p. 7 of the Office Action, Applicants provisionally elect, pursuant to the provisions of MPEP 803.02, and solely for the purpose of commencing examination under that section, compounds according to new claim 113 in which Q^3 is C(O) and Q^4 is CH₂. This group of compounds does not include a group Q^5 , and defines compounds having a common core structure, namely the seven-membered ring of formula "X" in claim 113. Q^1 and Q^2 define various functional groups which are generally similar to those defined by the M and R groups (in fact, Q^1 has the same definition as the R groups). The examiner did not indicate that election would be needed for the M and R groups; Applicants accordingly submit that election similarly is not required among these various functional groups.

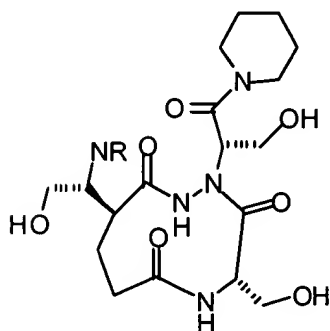
In addition Applicants do not agree with the statement that claims 74-90 (now 113-133) contain independent inventions and lack unity. These claims cover a series of compounds in Markush form, which is permitted under both International and United States practice, and for which examination as a whole is provided under MPEP 803.02. Applicants request that examination of these claims commence under that Section and, should the examiner not find invalidating art, continue past the provisionally elected compounds through the remainder of the claims.

The examiner asserts that the claims lack a technical feature because some compounds are known in the art, and cites publications by Kahn and Hanessian et al. in support. However, these references do not disclose compounds of the types claimed in the elected claims 113-133, as none of the compounds in these references can be produced by an expansion of formula "X" as described in the claims, nor from the intermediate compounds. For the convenience of the examiner the cited compounds from these references are shown below.

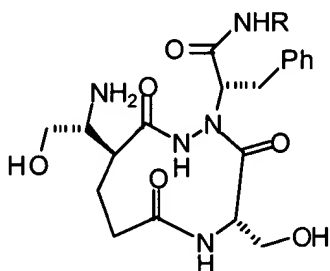
The seven compounds from the Kahn paper, numbers 17, 18, 23, 25-28 and E (see below) all contain an aza (N-N) function in the ring, which is not encompassed within the definition of the compounds in claim 113, as is the basic ring structure even without the N-N functionality. It is also impossible to specify any of the five 5,7-fused systems described in the Hanessian et al. reference (A-E below). There is no option in the claimed compounds for an exocyclic carboxylate at a bridgehead position (structures A and B), nor for fused benzene rings (C and D). Even at the most basic level of the C-N framework it is impossible to specify these 5,7 systems from formula "X".

Applicants submit that unity of invention therefore exists within the elected claims.

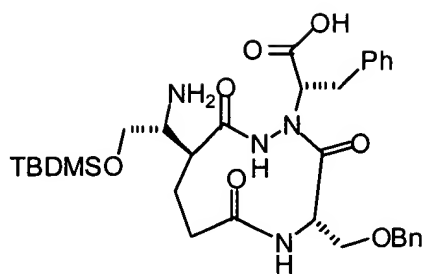
Proposed prior art structures.



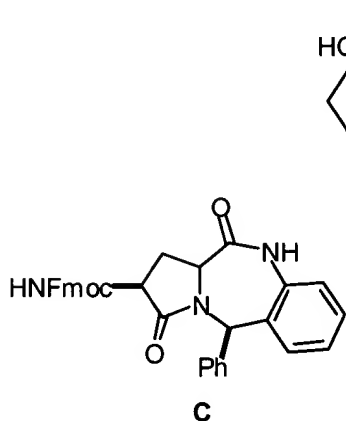
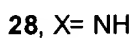
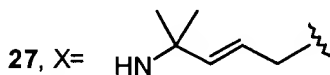
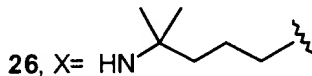
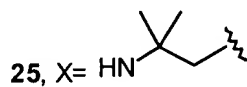
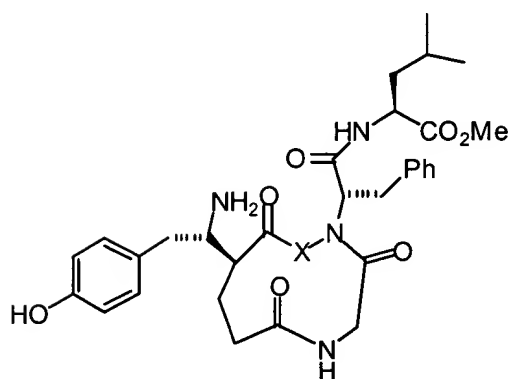
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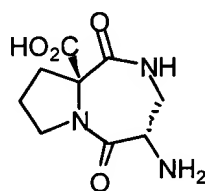
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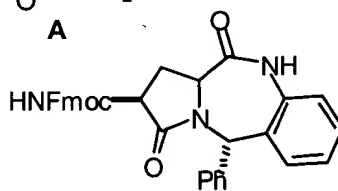
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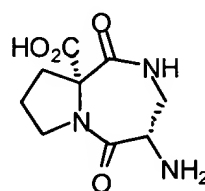
C



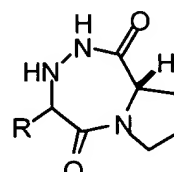
A



D



B



E

Appl. No. 09/647,054
Amdt. dated July 18, 2003
Reply to Office Action of February 21, 2003

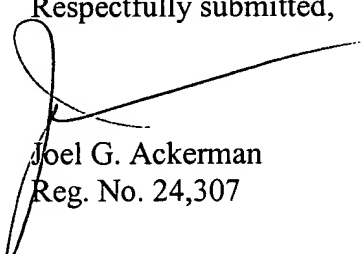
PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending and under examination in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned.

Respectfully submitted,



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APPENDIX A

AMENDED VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

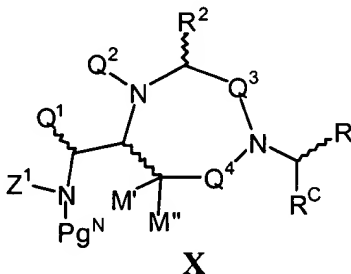
Please cancel claim 73, which has been replaced by new claim 108.

Please amend claim 108 to read as follows:

108. (Amended) A library of peptide mimetics comprising at least one mimetic from Claim 4 113.

Please cancel claims 74-94 and replace by new claims 113-133 as follows:

113. A general mimetic of the structure



wherein:

~~~~ indicates a bond at a chiral centre of the structure which centre may be in the R or S configuration or a mixture thereof;

R and R<sup>2</sup> is an amino acid side chain group which may be the same or different;

M' and M'' may be the same or different and are selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, chloro and C<sub>1</sub>-C<sub>4</sub> alkoxy;

Z' is selected from the group consisting of hydrogen, methyl and part of a cyclic amino acid sidechain joined to Q<sup>1</sup>

Pg<sup>N</sup> is a protecting group for amine;

$R^C$  is selected from the group consisting of a carboxy terminal part of the mimetic, hydrogen, R, and  $CH_2R$ ;

$Q^1 = R^1$  which has the same definition as R and  $R^2$  above and  $Q^2 = Z$  where Z is selected from the group consisting of hydrogen, methyl, ethyl, formyl and acetyl,  $-CH_2R$ , and  $C(O)R$  or alternatively Z is part of a cyclic amino acid sidechain group joined to  $R^2$ ; or  $Q^1$  and  $Q^2$  taken together represent a cyclic group;

$Q^3$  is selected from the group consisting of  $C(O)$  and  $CH_2$ ,  $-C(O)N(Q^5)CH(R)C(O)-$ ,  $-C(O)N(Q^5)CH(R)CH_2-$  wherein  $Q^5$  is a covalent bond from the  $Q^4$  group to the nitrogen atom in  $Q^3$  to form a bicyclic ring system;

$Q^4$  is selected from the group consisting of  $CH(M')$ ,  $C(O)$ ,  $CH(Q^5)CH_2$  and  $CH(Q^5)C(O)$ ; with the provisos that when:-

- (i)  $Q^3$  is  $C(O)$ , then  $Q^4 = CH(M')$ ;
- (ii)  $Q^3$  is  $CH_2$ , then  $Q^4 = C(O)$ ;
- (iii)  $Q^3$  is  $-C(O)N(Q^5)CH(R)C(O)-$ , then  $Q^4 = CH(Q^5)CH_2$ ;
- (iv)  $Q^3$  is  $-C(O)N(Q^5)CH(R)CH_2-$ , then  $Q^4 = CH(Q^5)C(O)$ ;

where  $Q^5$  is a covalent bond from the  $Q^4$  group to the nitrogen atom in  $Q^3$  which is a cyclization forming a bicyclic ring system.

114. A peptide mimetic as claimed in claim 113 wherein when  $Q^1$  and  $Q^2$  form a cyclic group  $Q^1Q^2$  which is selected from the group consisting of  $-CH(R)C(O)-$ ,  $-CH_2CH(R)C(O)-$ ,  $-CH_2CH_2CH(R)C(O)-$ ,  $-CH(R)CH_2-$ ,  $-CH_2CH(R)CH_2-$ ,  $-CH_2CH_2CH(R)CH_2-$ ,  $-CH_2CH(R)-$ ,  $-CH_2CH_2CH(R)-$ ,  $-CH(R)CH_2CH_2-$ ,  $-CH_2CH(R)CH_2CH_2-$ ,  $-CH(R)CH_2C(O)-$  and  $-CH_2CH(R)CH_2C(O)-$ .

115. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is  $C(O)$  or  $CH_2$ .

116. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is -C(O)N( $Q^5$ )CH(R)C(O)- or -C(O)N( $Q^5$ )CH(R)CH<sub>2</sub>-.

117. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is CH(R)C(O) $Q^2$ ,  $Q^1Q^2$ - forms a cyclic group -CH(R)C(O)- $Q^2$ ,  $Q^3$  is C(O) or CH<sub>2</sub>.

118. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is CH<sub>2</sub>CH(R)C(O) $Q^2$ ,  $Q^1Q^2$ - forms a cyclic group -CH<sub>2</sub>CH(R)C(O)-,  $Q^3$  is C(O) or CH<sub>2</sub>.

119. A peptide mimetic as claimed in Claim 113 wherein  $R^C$  is C(O)Pg<sup>C</sup> where Pg<sup>C</sup> is a protecting group for carboxylic acid.

120. A peptide mimetic as claimed in Claim 119 wherein Pg<sup>C</sup> is selected from the group consisting of alkoxy, benzyloxy, allyloxy, fluorenylmethyloxy amines forming easily removable amides, a cleavable linker to a solid support, the solid support, hydroxy, NHR, OR, R or the remaining C-terminal portion of the mimetic.

121. A peptide mimetic as claimed in Claim 113 wherein Pg<sup>N</sup> is selected from a group consisting of Boc, Cbz, Alloc, trityl, a cleavable linker to a solid support, the solid support, the solid support, hydrogen, R, C(O)R or part of the remaining N-terminal portion of the mimetic.

122. A peptide mimetic as claimed in Claim 113 wherein M' or M'' is methoxy.

123. A peptide mimetic as claimed in Claim 113 wherein M' or M'' is methyl.

124. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is R<sup>1</sup>,  $Q^2$  is hydrogen,  $Q^3$  is C(O), Z<sup>1</sup>=H and  $R^C$  is C(O)Pg<sup>C</sup>.

125. A peptide mimetic as claimed in Claim 124 where R<sup>1</sup> and R<sup>2</sup> ≠ H.



126. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is  $R^1$ ,  $Q^2$  is hydrogen,  $Q^3$  is  $CH_2$ ,  $Z^1=H$  and  $R^C$  is  $C(O)Pg^C$ .

127. A peptide mimetic as claimed in Claim 126 where  $R^1$  and  $R^2 \neq H$ .

128. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is  $R^1$ ,  $Q^2$  is hydrogen,  $Q^3$  is -  
 $C(O)N(Q^5)CH(R)C(O)-$ ,  $Z^1=H$  and  $R^C$  is  $C(O)Pg^C$ .

129. A peptide mimetic as claimed in Claim 113 wherein  $Q^1$  is  $R^1$ ,  $Q^2$  is hydrogen,  $Q^3$  is -  
 $C(O)N(Q^5)CH(R)CH_2-$ ,  $Z^1=H$  and  $R^C$  is  $C(O)Pg^C$ .

130. A peptide mimetic as claimed in Claim 114 wherein  $Q^1Q^2$  is  $-CH(R^2)C(O)-$ ,  $Q^3$  is  $C(O)$ ,  
 $Z^1=R^1$  and  $R^C$  is  $C(O)Pg^C$ .

131. A peptide mimetic as claimed in Claim 114 wherein  $Q^1Q^2$  is  $-CH(R^2)C(O)-$ ,  $Q^3$  is  $CH_2$ ,  
 $Z^1=R^1$  and  $R^C$  is  $C(O)Pg^C$ .

132. A peptide mimetic as claimed in Claim 114 wherein  $Q^1Q^2$  is  $-CH_2CH(R^2)C(O)-$ ,  $Q^3$  is  
 $C(O)$ ,  $Z^1=R^1$  and  $R^C$  is  $C(O)Pg^C$ .

133. A peptide mimetic as claimed in Claim 114 wherein  $Q^1Q^2$  is  $-CH_2CH(R^2)C(O)-$ ,  $Q^3$  is  
 $CH_2$ ,  $Z^1=R^1$  and  $R^C$  is  $C(O)Pg^C$ .